

ical device comprising of four individually calibrated elements attached onto foot-worn platforms and capable of unloading the diseased articular surface in knee osteoarthritis (OA) during standing and walking, simultaneously training neuromuscular control by controlled biomechanical perturbations.

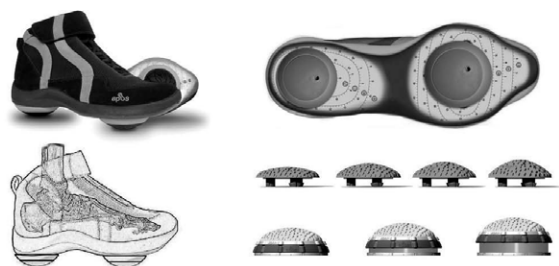
The purpose of this study was to examine the effectiveness of APOS system in reducing pain and improving function in knee OA patients one year following the original study.

**Methods:** *Patients:* A Total of 37 patients out of 58 patients from the original study volunteered to continue the follow-up for additional 12 month (23 patients from the original study active group and 14 patients from the original study control group, who started active treatment at original study endpoint). Patients were followed from October 2005 to January 2007.

*Interventions:* Patients continued the treatment with the device that had been individually calibrated to accommodate a diminished-pain joint alignment.

The patients were assessed during the follow up study at 6 month and 12 month after the original study ended. Primary outcome measures were the WOMAC index and the Aggregated Locomotor Function (ALF) assessment.

**Results:** At 12 months, the active group maintained significant pain relief and improved function similar to the active group results at the end of the original study which showed a decrease of 3.68 on the WOMAC scale ( $P < 0.001$ ), representing a mean improvement of 66.8%, and a decrease of 14 on the ALF scale ( $P < 0.001$ ), representing a mean improvement of 37.4%.



**Conclusions:** The findings demonstrate that APOS system is effective and significantly reduce pain and improve function among knee OA patients.

## Bone Biology

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### SUBCHONDRAL BONE CHANGES AND CARTILAGE DEGENERATION ARE DIFFERENTIALLY REGULATED; COMPARISON OF TWO CANINE MODELS OF OSTEOARTHRITIS

**F. Intema**<sup>1</sup>, **Y. Sniekers**<sup>2</sup>, **S.A. Yocum**<sup>3</sup>, **A. Zuurmond**<sup>4</sup>, **J. DeGroot**<sup>3</sup>, **S.C. Mastbergen**<sup>1</sup>, **H. Weinans**<sup>2</sup>, **F.P. Lafeber**<sup>1</sup>  
<sup>1</sup>Rheumatology & Clinical Immunology, University Medical Center Utrecht, Utrecht, The Netherlands; <sup>2</sup>Orthopedics, Erasmus Medical Center, Rotterdam, The Netherlands; <sup>3</sup>TNO Quality of Life, Leiden, The Netherlands; <sup>4</sup>Pfizer Inc PGRD, Ann Arbor, MI

**Purpose:** In the present study peri-articular bone changes in two experimentally induced canine models of osteoarthritis (OA) are evaluated. Whereas the anterior cruciate ligament transaction (ACLT) model depends on permanent joint instability to induce features of OA, the Groove model depends on surgically applied femoral cartilage damage accompanied by transient intermittent intensified loading of the affected joint. Importantly, the tibial plateau is surgically untouched. In both models degenerative

cartilage changes are progressive over time, very similar, and mimic human features of OA. In the Groove model, in contrast to the ACLT model, synovial inflammation is minimal and diminishes over time. In both models cartilage degeneration has extensively been studied by use of histochemistry and biochemical parameters of proteoglycan turnover. In the present study the changes in peri-articular bone in these two canine models of OA have been evaluated using micro-CT.

**Methods:** 20 weeks post surgery (bilateral OA induction), tibial plateaus were evaluated ( $n=6$  animals for both models) and compared to those of sham-operated dogs ( $n=6$ ). The tibial plateau was chosen because the tibial cartilage surface was unaffected during surgery in the Groove model. Cartilage was analyzed and architecture of subchondral plate and trabecular (epiphyseal) bone as well as of metaphyseal bone was quantified using micro-CT.

**Results:** Cartilage macroscopy, histology and biochemical analysis demonstrated the significant characteristic features of osteoarthritis for both the ACLT and Groove model not statistically significantly different between both models. Trabecular bone volume fraction (BV/TV) decreased -6% for the Groove (ns) and -31% ( $p < 0.05$ ) for the ACLT model and trabecular thickness (TbTh) showed a decrease of -5% for the Groove (ns) and -25% ( $p < 0.05$ ) for the ACLT model. Also structure model index (SMI) and connectivity density (CD) showed an increase for the ACLT model ( $p < 0.05$ ) but not in the Groove model (ns). In contrast to the difference between both models for these trabecular parameters, the subchondral plate thickness reduced for both models statistically significantly (-27% and -46% for the Groove and ACLT model; both  $p < 0.05$ ). Interestingly, in the ACLT model structural changes in the subchondral trabecular bone were found to be very similar in the metaphysis at a significant distance from the joint, suggesting disuse of the extremity due to the induction of OA. This was not observed for the Groove model.

**Conclusions:** While osteoarthritic features in cartilage were equal for the Groove and ACLT model as was the decrease in subchondral plate thickness. Peri-articular trabecular bone changes were statistically significantly more outspoken in the ACLT model and observed concomitantly with similar trabecular bone changes further away from the joint suggesting unloading of the affected joint. This demonstrates that the interaction between cartilage and bone in the process of OA can be differentially regulated, depending on the cause of OA (in this study the type of model used), and that disuse induced bone changes should be taken into account when evaluating OA related bone changes.

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### MECHANICAL STRESS STRONGLY INDUCES INTERLEUKIN-6 PRODUCTION BY OSTEOBLASTS: A NEW *IN VITRO* 3D COMPRESSION MODEL

**C. Sanchez**<sup>1</sup>, **O. Gabay**<sup>2</sup>, **C. Salvat**<sup>2</sup>, **Y. Henrotin**<sup>1</sup>, **F. Berenbaum**<sup>2</sup>

<sup>1</sup>University of Liège, Liège, Belgium; <sup>2</sup>University Pierre et Marie Curie, Paris, France

**Purpose:** To study mechanical stress on a new model of osteoblast compression in their own-produced collagen matrix

**Methods:** Primary calvaria osteoblasts were isolated from new born mice and cultured for 28 days in monolayer. At the end of this period, osteoblasts were embedded in their abundant and newly synthesized collagen matrix. This collagen membrane containing osteoblasts was then submitted to compression in Biopress Flexercell plates (6 to 10% compression at 1Hz frequency) during 1 to 8 h. The expression of 20 genes was investigated by real time RT-PCR. Interleukin (IL)-6, matrix metalloproteinase (MMP)-3 and prostaglandin (PG)<sub>E2</sub> were assayed in the culture medium by immunoassays